

REMARKS

I. Status of the claims and amendments

Claims 1 and 4-14 are pending in this application. Claims 2 and 3 were cancelled in a previous response. No claim has been amended in this response.

II. Rejection under 35 U.S.C. § 103

The Office rejected claims 1 and 4-14 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication No. 2003/0123057 ("*Lemmo*"), in view of Bizid et al., Structure by diffraction of X-rays of liquid gallium between +50 and 110°C, *Phys. Stat. Sol. (a)* 23:135-145 (1974) ("*Bizid*"). Office Action at 4.

The Office indicates that "[i]ndependent instant claims 1 and 4, and corresponding dependent instant claims 5-10 and 14 recite a method comprising of comparing a PDF [pairwise distribution function] trace of a first sample of a substance, wherein the substance is a pharmaceutical, with a PDF trace of a second sample of the substance to identify any similar or different solid forms." *Id.* at 4.

In the Office's view, *Lemmo* "discloses a method of screening an array of samples and determining if any share spectral features, which is similar to comparing diffraction patterns, in paragraphs [0017] and [0021]-[0022], as well as the use of X-ray diffraction analysis in paragraph [0041]." *Id.* at 7. The Office argues that *Lemmo* "further discloses that compounds of interest for analysis includes pharmaceuticals in paragraph [0076], and recites the use of a computer in a system for detecting similarities among a plurality of samples in claims 8-21." *Id.* at 7-8.

The Office acknowledges that *Lemmo* "does not expressly disclose the use of pair distribution function, PDF," but argues that *Bizid* "discloses an X-ray diffraction study wherein PDF is employed for comparative analysis of different physical phases of a gallium sample in the English Abstract." *Id.* at 8. According to the Office, "[s]ince both [*Lemmo*] and [*Bizid*] focus of [sic] the field of X-ray diffraction, it would have been obvious to one of ordinary skill in the art to employ PDF with X-ray diffraction analysis for the purpose of comparing liquid and crystalline forms of a sample (English Abstract of BIZID et al.)" *Id.* Applicants respectfully traverse this rejection.

The pending claims are directed to: a) methods of "comparing the PDF traces" of pharmaceutical compounds to determine whether the pharmaceutical compounds are the same or different (*see, e.g.*, independent claims 1 and 4); b) methods of screening using PDF traces (*see, e.g.*, independent claim 11); c) methods using PDF traces and a hierarchical cluster analysis for comparisons of substances (*see, e.g.*, independent claim 12); and d) a system with means for performing comparisons using PDF traces (*see, e.g.*, independent claim 13).

As the Examiner acknowledges, *Lemmo* does not disclose the use of the PDF transform. Office Action at 5. Rather, *Lemmo* discloses x-ray powder diffraction to analyze samples in, for example, a screen. The Office turns to *Bizid* arguing that it provides the necessary use of PDF rendering the instant application obvious to one of ordinary skill in the art. *Id.* Applicants respectfully disagree with the Office's characterization of *Bizid*.

The PDF has been used by physicists to understand the nature of simple inorganic materials such as elements. For example, *Bizid* is directed to the study of

elemental gallium using PDF (called radial distribution function by *Bizid*), as a function of temperature. *Bizid* at Abstract. It is worth noting that, as the title of the reference indicates, part of the study focuses on gallium in the liquid phase. *Bizid* collected PDF data at different temperatures to gain an understanding about the internal structure of gallium. *Id.* Upon cooling the gallium, *Bizid* also collected x-ray diffraction data on the material. *Id.* The authors concluded that when liquid gallium cools, the PDF data shows nearest-neighbor interactions similar to metastable crystalline phases rather than to the most stable crystalline phase of gallium. *Id.*

Thus, *Bizid* teaches the use of PDF methods to compare data collected on a *liquid* phase of a *known* elemental metal, with another phase of the same, *known* elemental metal. Nowhere does *Bizid* suggest that the PDF could be used, as recited in the instant claims, to compare different samples of a substance to establish whether the substances are the same or different solid forms. Further, there is no indication in the references cited that the PDF could be used on pharmaceutical substances, which gallium clearly is not.

Moreover, *Bizid* teaches that x-ray data and PDF data give inconsistent results. For example, *Bizid* teaches that the x-ray diffraction data yield a different result than the PDF data on gallium as a function of temperature. In particular, *Bizid* teaches that "a secondary peak, associated with the main peak, becomes more and more important as the temperature decreases" Abstract. This is in contrast to the PDF data which, according to *Bizid*, "do not indicate, however, any notable change with the temperature." *Id.* In other words, the two different analytical techniques reach opposite conclusions about the system under study. In such a circumstance, one of ordinary skill in the art

would have no reason to alter the teachings of *Lemmo*. Indeed, one of ordinary skill in the art would have no incentive to modify *Lemmo*, which teaches the use of x-ray powder diffraction data, to compare, for example, solid forms with the PDF analytical technique of *Bizid*, which: (a) is directed to gallium (not a pharmaceutical substance), (b) focuses on the analysis of the internal structure of gallium as a function of temperature, and (c) teaches that the PDF yields a different conclusion about the gallium than x-ray powder diffraction.

For at least these reasons, the Office has not made a *prima facie* case of obviousness and Applicants respectfully traverse the rejection.

III. Conclusion

In view of the foregoing remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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